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EXAMINER

FORMAN, BETTY J

ART UNIT	PAPER NUMBER
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1634

DATE MAILED: 06/21/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/776,252

Applicant(s)

ELLINGTON, ANDREW

Examiner

BJ Forman

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 07 April 2005.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 29-43 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 29-43 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

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FINAL ACTION

Status of the Claims

1. This action is in response to papers filed 7 April 2005 in which an Information Disclosure Statement was submitted, all previously examined claims were canceled and new claims 29-43 were added. The amendments have been thoroughly reviewed and entered.

The previous rejections in the Office Action dated 7 December 2004 **are withdrawn in view of the amendments**. Applicant's arguments have been thoroughly reviewed and are discussed below. New grounds for rejection, necessitated by the amendments and IDS, are discussed.

Claims 29-43 are under prosecution.

Information Disclosure Statement

2. The references listed on the 1449 received 7 April 2005 have been reviewed and considered. The references that are crossed out on the 1449 were previously reviewed and considered as indicated on earlier 1449s and 892s.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 29-43 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

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Claims 29-43 are indefinite in Claim 1 for the recitations "the unbound state" and "the differential signal" because the recitations lack proper antecedent basis. It is suggested that the claim be amended to correct e.g. replace "the" with "a".

Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

6. Claims 29-37, 40-43 are rejected under 35 U.S.C. 102(e) as being anticipated by Stanton et al (U.S. Patent No. 6,680,377 having priority to 60/134,330 filed 14 May 1999).

Regarding Claim 1, Stanton et al teach a method of transducing a conformational change of a signaling aptamer upon ligand binding, the method comprising the steps of providing a aptamer comprising a covalently coupled reporter (#24) wherein in the unbound state an optical signal produced by the aptamer is less than (i.e. quenched) relative to the signal produced upon the conformational change resulting from ligand binding; contacting the aptamer with the ligand and detecting the differential signal produced as a result of the conformational change (Column 12, lines 34-67 and Example 1, Column 22, lines 40-Column 23, line 30).

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Regarding Claim 30, Stanton et al disclose the method further comprising the step of quantitating the amount of ligand bound (Column 19, lines 39-46 and 61-67).

Regarding Claim 31, Stanton et al disclose the method wherein the detection is fluorescence (Column 5, lines 44-60).

Regarding Claim 32, Stanton et al disclose the method wherein the coupling occurs during chemical synthesis or post-transcription (Column 9, lines 50-58).

Regarding Claim 33, Stanton et al disclose the reporter is a dye (Column 9, line 50).

Regarding Claim 34, Stanton et al disclose the reporter is fluorescent dye (Column 9, line 61).

Regarding Claim 35, Stanton et al disclose the method wherein the reporter replaces a nucleic acid residue (Column 13, lines 1-10)

Regarding Claim 36, Stanton et al disclose the reporter is fluorescein (Column 13, lines 1-5).

Regarding Claim 37, Stanton et al disclose the method wherein the aptamer is RNA, DNA, modified RNA or modified DNA (Column 3, lines 59-64).

Regarding Claim 40, Stanton et al disclose the method wherein dye replaces a residue adjacent to ligand binding site (Fig. 3c-d).

Regarding Claim 41, Stanton et al disclose the ligand is in solution i.e. the sample containing the ligand is dissolved in saline buffer (Column 22, lines 63-67).

Regarding Claim 42, Stanton et al disclose the method wherein the ligand is immobilized on a support (Column 22, lines 59-62).

Regarding Claim 43, Stanton et al disclose the method wherein the ligand is immobilized on a chip i.e. glass slide (Column 22, lines 59-62).

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7. Claims 29-37, 40-41 are rejected under 35 U.S.C. 102(b) as being anticipated by Royer (U.S. Patent No. 5,445,935, issued 29 August 1995).

Regarding Claim 29, Royer discloses a method for transducing a conformational change (i.e. complex formation) in a signaling aptamer, the method comprising, providing a signaling aptamer comprising a reporter covalently coupled to an aptamer (e.g. labeled DNA, Column 6, lines 34-50) wherein in the unbound state an optical signal produced by the aptamer is less than (i.e. quenched) relative to the signal produced upon the conformational change resulting from ligand binding (Column 4, lines 21-28); contacting the aptamer with the ligand and detecting the differential signal produced as a result of the conformational change i.e. protein ligand-oligonucleotide aptamer binding results in complex formation (Column 3, lines 42-53; Fig. 3; and Claim 1).

The instant specification defines the claimed aptamers: "As used herein, the term "Aptamer" or "selected nucleic acid binding species" shall include non-modified or chemically modified RNA or DNA." (Page 14, lines 7-10)

The instant specification defines the claimed conformational change: "As used herein, the term "conformational changes" shall include, but is not limited to, changes in spatial arrangements including subtle changes in chemical environment without a concomitant spatial arrangement." (page 15, lines 17-20)

While limitations from the specification are not read into the claims, the complex formation resulting from protein-oligonucleotide binding is encompassed by the aptamer and conformational change as defined by the specification.

Regarding Claim 30, Royer disclose the method further comprising quantitating the amount of ligand bound to the aptamer (Column 4, lines 46-52).

Regarding Claim 31, Royer discloses the method wherein the optical signal is polarization (Abstract).

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Regarding Claim 32, Royer discloses the method wherein the covalent coupling of the reporter occurs during synthesis or post transcriptionally (Column 6, lines 34-47).

Regarding Claim 33, Royer discloses the method wherein the reporter is a dye (Column 4, line 63-Column 5, line 6 and Column 6, lines 63-65).

Regarding Claim 34, Royer discloses the method wherein the dye is a fluorescent dye (Column 4, line 63-Column 5, line 6 and Column 6, lines 63-65).

Regarding Claim 35, Royer discloses the method wherein the dye is inserted between two nucleic acid residues (Column 6, line 36-38).

Regarding Claim 36, Royer discloses the method wherein the dye is fluorescein (Column 6, lines 63-65).

Regarding Claim 37, Royer discloses the method wherein the signaling aptmer comprises DNA or RNA (Column 6, lines 48-50).

Regarding Claim 40, Royer discloses the method wherein the dye is inserted between two nucleic acid residues (Column 6, line 36-38). The claim does not define or limit required by the phrase "functional nucleic acid residue". The nucleic acids of Royer are part of a part of an oligonucleotide probe. Each nucleotide of the probe has some functionality and therefore meet the requirements of the non-specific functionality as claimed.

Regarding Claim 41, Royer disclose the method wherein the aptamer is in solution (Column 4, lines 10-14).

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having

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ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

9. Claims 38-39 are rejected under 35 U.S.C. 103(a) as being unpatentable over Stanton et al (U.S. Patent No. 6,680,377 having priority to 60/134,330 filed 14 May 1999) in view of Szostak et al. (U.S. Patent No. 5,631,146, issued 20 May 1997).

Regarding Claims 38-39, Stanton et al teach a method of transducing a conformational change of a signaling aptamer upon ligand binding, the method comprising the steps of covalently coupling a reporter (#24) within an aptamer in proximity to ligand binding site, such that the reporter does not interfere with binding (Fig. 3c-d) wherein reporter replaces a nucleic acid residue (Column 13, lines 1-10) and wherein the ligand is not a nucleic acid molecule (Column 3, lines 56-64). Stanton et al teach the method further comprising placing the aptamer in solution, contacting the aptamer with the ligand to bind ligand to the aptamer, thereby inducing conformational change in the aptamer and transducing the change to a detectable signal increase generated by the reporter (Column 12, lines 34-67 and Example 1, Column 22, lines 40-Column 23, line 30). While Stanton et al immobilize the aptamer, their contacting is performed in solution as claimed (Column 22, lines 63-67).

Stanton et al teach their method is useful for the isolate of various non-nucleic acid target molecules (Column 3, lines 56-59) but they do not teach the aptamers are anti-adenosine RNA or DNA aptamer wherein the former is ATP-R-ACI3 and the latter is DFL7-8 and the ligand (target molecule) is adenosine.

However, Szostak et al teach anti-adenosine triphosphate and anti-adenosine DNA aptamers prepared by the same process (Column 4, line 56-column 6, line 9) and they further teach anti-adenosine aptamers are especially useful for ATP purification and in vivo quantification (Column 18, lines 31-42). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply anti-adenosine aptamers of Szostak et al to the target detection of Stanton et al for the expected benefits of purification and

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in vivo quantification of an important target molecule as taught by Szostak et al (Column 18, lines 31-42).

Response to Arguments

10. Applicant asserts that the aptamers of Stanton differ from those claimed because the during the unbound state, the change in signal results from an appended quencher.

Applicant asserts that the instantly claimed signal change results from the conformational change of the aptamer and does not require a quencher as required by Stanton. The argument has been considered but is not found persuasive because the claimed method merely requires a signal change resulting from conformational change. Stanton specifically teaches the conformational change produces a signal change i.e. upon ligand binding, the conformation of the aptamer changes whereby their quencher can no longer quench the reporter. The additional quencher molecule of Stanton is encompassed by the open claim language i.e. "a signaling aptamer comprising a reporter". Because Stanton teaches aptamer-ligand binding causes a conformational change in the aptamer resulting in increased signal, Stanton teaches the method as claimed.

Applicant asserts that the instant invention provides the advantage of not requiring modification of the aptamer's primary sequence. The advantage is noted. However, the asserted advantage is not commensurate in scope with the instant claims.

11. Applicant's amendment and IDS necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO

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MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Conclusion

12. No claim is allowed.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to BJ Forman whose telephone number is (571) 272-0741. The examiner can normally be reached on 6:00 TO 3:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones can be reached on (571) 272-0745. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

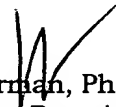
Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system

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For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.



BJ Forman, Ph.D.
Primary Examiner
Art Unit: 1634
June 17, 2005